

Interview 2/19/04

DOCKET NO.: TIBO-0010
 Application N. : 09/633,232
 Office Action Dated: November 3, 2003

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 REPLY FILED UNDER EXPEDITED
 PROCEDURE PURSUANT TO
 37 CFR § 1.116

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-6 (cancelled)

Claim 7 (currently amended) ~~The method of claim 5, wherein said cell is labeled by transfecting said cell with a DNA molecule encoding said A method of monitoring at least one cell or tissue in a biological system comprising:~~

- a) providing said biological system comprising said at least one cell or tissue;
 - b) labeling said at least one cell or tissue with at least one apo metal binding protein;
 - c) providing conditions which permit said at least one apo metal binding protein to emit a signal;
 - d) observing or measuring the signal; and
 - e) monitoring said at least one cell or tissue based on the signal observed or measured;
- wherein the cell is labeled by introducing into said cell a DNA molecule encoding said at least one apo metal binding protein.

Claims 8-10 (cancelled)

Claim 11 (withdrawn) A method of determining the cytotoxicity of a drug of interest comprising

- a) exposing at least one cell to the drug of interest;
- b) monitoring the at least one cell using the method of claim 5;
- c) determine the cytotoxicity of the drug of interest by determining whether the at least one cell is influenced by the drug of interest.

Claims 12-13 (cancelled)

Claim 14 (currently amended) ~~The method of claim 7, wherein said protein is labeled by preparing a fusion protein with said protein and A method of monitoring at least one cell or tissue in a biological system comprising:~~

- a) providing said biological system comprising said at least one cell or tissue;
- b) labeling said at least one cell or tissue with at least one apo metal binding protein;
- c) providing conditions which permit said at least one apo metal binding protein to emit a signal;

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- d) observing or measuring the signal; and
- e) monitoring said at least one cell or tissue based on the signal observed or measured;
wherein the cell is labeled by introducing into said cell a DNA molecule encoding a fusion
protein comprising at least one apo metal binding protein.

Claims 15-16 (cancelled)

Claim 17 (currently amended) The method of claim 15, A method of monitoring at least one cell or tissue in a biological system comprising:

- a) providing said biological system comprising said at least one cell or tissue;
- b) labeling said at least one cell or tissue with at least one apo metal binding protein;
- c) providing conditions which permit said at least one apo metal binding protein to emit a signal;
- d) observing or measuring the signal; and
- e) monitoring said at least one cell or tissue based on the signal observed or measured;

wherein said conditions which permit said at least one apo metal binding protein to emit a signal comprise providing at least one metal which binds to said at least one apo metal binding protein; wherein said apo metal binding protein is a blue copper protein chosen from azurin, pseudo-azurin, a plastocyanin, and a phytoeyanin.

Claim 18 (withdrawn) The method of claim 5, wherein said copper binding protein is blue oxidase chosen from ascorbate oxidase, ceruloplasmin, and laccase.

Claim 19 (withdrawn) The method of claim 5, wherein said copper binding protein is a nitrite reductase.

Claim 20 (withdrawn) The method of claim 1, wherein said at least one apo metal binding protein is chosen from haemoglobin, catalase and transferrin.

Claim 21 (withdrawn) A method of labeling at least one protein of interest comprising fusing the at least one protein of interest to at least one apo metal binding protein.

Claim 22 (withdrawn) A method of labeling a cell of interest comprising introducing into said cell of interest at least one apo metal binding protein or binding to the membrane of said cell of interest at least one apo metal binding protein.

Claim 23 (withdrawn) The method of labeling a cell of interest according to claim 22, wherein the step of introducing at least one apo metal binding protein into said cell of interest is accomplished by transfecting said cell of interest with a gene encoding said at least one apo metal binding.

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Claim 24 (withdrawn) A method for detecting at least one cell expressing a protein of interest comprising

- a) introducing into said at least one cell a DNA molecule having a DNA sequence encoding the protein of interest and an additional DNA molecule having a DNA sequence encoding at least one apo metal binding protein;
- b) providing conditions which permit expression of the at least one apo metal binding protein and the protein of interest;
- c) providing conditions which permit the at least one apo metal binding protein to emit a signal; and
- d) detecting the cell expressing the protein of interest by observing or measuring the signal of the at least one apo metal binding protein.

Claim 25 (withdrawn) The method of claim 24, wherein said DNA molecule and said additional DNA molecule are linked.

Claim 26 (withdrawn) The method of claim 24, wherein said cell is chosen from bacterial, fungal, plant or animal cell.

Claim 27 (withdrawn) A method for localizing at least one protein of interest in a cell comprising

- a) introducing into said cell a DNA molecule comprising
- b) a DNA sequence encoding the at least one protein of interest, linked to an additional DNA sequence encoding at least one apo metal binding protein such that the protein produced by the DNA molecule will have the at least one protein of interest fused to the at least one apo metal binding protein.;
- c) providing conditions which permit expression of the fused protein;
- d) providing conditions which permit the at least one apo metal binding protein to emit a signal; and
- e) determining the location of the fused protein from the signal, thereby localizing the protein of interest in the cell.

Claim 28 (withdrawn) A method of designing a therapeutic agent for treating a disease comprising:

- a) labeling at least one cell that is a target of the disease with at least one apo metal binding protein;
- b) providing conditions which permit said at least one apo metal binding protein to emit a signal;

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- c) observing or measuring the signal;
- d) determining whether the therapeutic agent is effective treating the disease by monitoring the signal observed or measured from the cell.

Claim 29 (withdrawn) A method of designing a therapeutic agent for treating a virus or bacterial infection comprising:

- a) labeling the virus or the bacteria with at least one apo metal binding protein;
- b) providing conditions which permit said at least one apo metal binding protein to emit a signal;
- c) observing or measuring the signal;
- d) determining whether the therapeutic agent is effective treating the virus or bacterial infection by monitoring the signal observed or measured from the virus or the bacteria.

Claim 30 (withdrawn) The method according to claim 29, wherein said virus is the HIV virus.

Claim 31 (withdrawn) A eucaryotic cell comprising a DNA sequence encoding at least one copper binding protein.

Claim 32 (withdrawn) The eucaryotic cell of claim 31, wherein said eucaryotic cell is an animal cell.

Claim 33 (withdrawn) The eucaryotic cell of claim 31, wherein said DNA sequence comprises the azu gene.

Claim 34 (withdrawn) The eucaryotic cell of claim 33, wherein said at least one blue copper protein is azurin.

Claim 35 (withdrawn) A kit for monitoring at least one target substance in a biological system comprising at least one apo metal binding protein.

Claim 36 (previously presented) A method of monitoring at least one target substance in a biological system comprising:

- a) providing said biological system comprising said at least one target substance, wherein said at least one target substance is a cell that is labeled by transfecting said cell with a DNA molecule encoding said at least one apo metal binding protein;
- b) labeling said at least one target substance with at least one apo metal binding protein, wherein said apo metal binding protein is a protein capable of binding itself to said metal;
- c) providing conditions which permit said at least one apo metal binding protein to emit a signal;

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- d) observing or measuring the signal; and
- e) monitoring said at least one target substance based on the signal observed or measured.

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Claim 37 (previously presented) The method of claim 36, wherein said protein is labeled by preparing a fusion protein with said protein and at least one apo metal binding protein.

Claim 38 (previously presented) A method of monitoring at least one target substance in a biological system comprising:

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- a) providing said biological system comprising said at least one target substance;
 - b) labeling said at least one target substance with at least one apo metal binding protein, wherein said apo metal binding protein is a blue copper protein, and said blue copper protein is chosen from azurin, pseudo-azurin, a plastocyanin, and a phytocyanin;
 - c) providing conditions which permit said at least one apo metal binding protein to emit a signal, wherein said conditions which permit said at least one apo metal binding protein to emit a signal comprise providing at least one metal which binds to said at least one apo metal binding protein;
 - d) observing or measuring the signal; and
 - e) monitoring said at least one target substance based on the signal observed or measured.